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Commentary on Yagi

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Review of the pre- and post-marketing studies of zonisamide in Japan provides valuable insight into the optimal use of this drug; in particular, its efficacy in specific seizure subtypes.

After reviewing the data, Dr. Yagi has teased out some important distinctions regarding epilepsy and seizure subtypes. In particular, clinical trial results for patients who have temporal versus non-temporal lobe epilepsy are not usually separated out, as was done in Dr. Yagi's report. In animals, hippocampal and non-hippocampal areas differ in seizure-kindling threshold and density of receptors; both of which serve as sites of action for many antiepilepsy drugs (AEDs). In clinical trials, patients tend to be lumped together for analysis, and distinctions are not drawn about whether the agent being studied is more effective in one type of seizure over another. For this reason it is not clear whether some AEDs are more effective in some types of partial seizures. Dr. Yagi's analysis provides some useful direction for future reporting of clinical trial results.

The most remarkable findings in these studies of zonisamide are among patients with secondarily generalized epilepsy. Patients with atypical absence seizures appeared to do extremely well on zonisamide. Those with atonic seizures and Lennox–Gastaut syndrome also did well.

In the post-marketing study of newly diagnosed patients, there was an excellent efficacy rate, 93%, in patients with tonic seizures. These seizures are difficult to control. One area of concern with drugs that have a narrower spectrum of action than zonisamide, such as gabapentin and tiagabine, is that patients with generalized seizures often get worse while taking these agents. Among zonisamide-treated patients, there were very few instances of seizures worsening.

The case studies presented are instructive. Clinicians usually receive information from clinical trials that report results for large patient groups; however, subsets or individual patients often have a remarkable response to one drug over another, and this information can be useful. It was interesting to note that the best results among these three patients were achieved with zonisamide monotherapy.

The addition of zonisamide to the US market will help to optimize our management of patients with epilepsy. It will allow us to further expand our repertoire of drug combinations with complementary mechanisms of action, as well as to initiate monotherapy with zonisamide in appropriate situations.

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